

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference X16230	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US2004/018921	International filing date (day/month/year) 07/06/2004	(Earliest) Priority Date (day/month/year) 09/07/2003
Applicant ELI LILLY AND COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

TGF- β 1 LIGANDS

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-32 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-32 partially

anti TGF-b1 binding composition "1021" characterized by one or more of the following CDRs:

HC CDR1= Seq ID No: 13,

HC CDR2= Seq ID No: 14,

HC CDR3= Seq ID No: 15,

LC CDR1= Seq ID No: 22,

LC CDR2= Seq ID No: 23,

LC CDR3= Seq ID No: 24,

LC v-region (Seq ID No: 2) comprises Seq ID No: 22,23,24 and

HC v-region (Seq ID No: 4) comprises Seq ID No: 13,14,15

2. claims: 1-32 partially

anti TGF-b1 binding composition "2471" characterized by one or more of the following CDRs:

HC CDR1= Seq ID No: 16,

HC CDR2= Seq ID No: 17,

HC CDR3= Seq ID No: 18,

LC CDR1= Seq ID No: 25,

LC CDR2= Seq ID No: 26,

LC CDR3= Seq ID No: 27

3. claims: 1-32 partially

anti TGF-b1 binding composition "3821" characterized by:

HC CDR1= Seq ID No: 19,

HC CDR2= Seq ID No: 20,

HC CDR3= Seq ID No: 21,

LC CDR1= Seq ID No: 28,

LC CDR2= Seq ID No: 29,

LC CDR3= Seq ID No: 30,

LC v-region (Seq ID No: 10) comprises Seq ID No: 28,29,30 and

HC v-region (Seq ID No: 12) comprises Seq ID No: 19,20,21

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, EMBASE, BIOSIS, PAJ, LIFESCIENCES, SCISEARCH, CHEM ABS Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>✓ WO 00/66631 A (CAMBRIDGE ANTIBODY TECH ; TEMPEST PHILIP RONALD (GB); BRADDOCK PETA SA) 9 November 2000 (2000-11-09) ; page 1 - page 3 ; table 2 ; figures 1,4 ; examples 1,3,6</p> <p style="text-align: center;">----- -/--</p>	1-32

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

19 January 2005

Date of mailing of the international search report

07. 07. 2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Voigt-Ritzer, H

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>✓ SHAH M ET AL: "NEUTRALISATION OF TGF-BETA1 AND TGF-BETA2 OR EXOGENOUS ADDITION OF TGF-BETA3 TO CUTANEOUS RAT WOUNDS REDUCES SCARRING"</p> <p>JOURNAL OF CELL SCIENCE, CAMBRIDGE UNIVERSITY PRESS, LONDON, GB, vol. 108, no. PART 3, 1 March 1995 (1995-03-01), pages 985-1002, XP000609005</p> <p>ISSN: 0021-9533</p> <p>page 997, column 1, paragraph 2</p> <p>table 1</p>	1-13,30
X	<p>-----</p> <p>✓ Monoclonal anti-TGF-b1 antibody. R&D Systems, Ordering Information, Catalog Number: MAB2401, 29.1.2003.</p> <p>XP002313281</p> <p>abstract</p>	1-32
X	<p>-----</p> <p>✓ LUCAS C ET AL: "THE AUTOCRINE PRODUCTION OF TRANSFORMING GROWTH FACTOR-BETA1 DURING LUMPHOCYTE ACTIVATION A STUDY WITH A MONOCLONAL ANTIBODY-BASED ELISA"</p> <p>JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 145, 1 September 1990 (1990-09-01), pages 1415-1422, XP000917385</p> <p>ISSN: 0022-1767</p> <p>abstract</p> <p>page 1419, column 2, paragraph 2 - page 1420, column 1, paragraph 1</p> <p>figure 3</p>	1-14, 18-27, 30,31
X	<p>-----</p> <p>✓ WO 97/13844 A (CAMBRIDGE ANTIBODY TECH ; TEMPEST PHILIP RONALD (GB); THOMSON JULIA EL) 17 April 1997 (1997-04-17)</p> <p>page 12, line 12 - line 27</p> <p>figures 1bii,1ci</p> <p>examples 1,3,4,9</p> <p>page 62, line 25 - page 63, line 14</p> <p>page 67, line 12 - page 68, line 5</p> <p>page 100, line 4 - page 101, line 15</p>	1-32
X	<p>-----</p> <p>✓ FLANDERS K C ET AL: "ANTIBODIES TO PEPTIDE DETERMINANTS IN TRANSFORMING GROWTH FACTOR BETA AND THEIR APPLICATIONS"</p> <p>BIOCHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, PA, US, vol. 27, 1988, pages 739-746, XP002044723</p> <p>ISSN: 0006-2960</p> <p>page 744, column 2, paragraph 2</p> <p>figure 7</p> <p>-----</p> <p style="text-align: center;">-/--</p>	1-13,30

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>✓ ELLINGSWORTH L R ET AL: "TRANSFORMING GROWTH FACTOR-BETAS ARE EQUIPOTENT GROWTH INHIBITORS OF INTERLEUKIN-1-INDUCED THYMOCYTE PROLIFERATION" CELLULAR IMMUNOLOGY, vol. 114, no. 1, 1988, pages 41-54, XP009042444 ISSN: 0008-8749 page 43, paragraph 3 figures 6,7,9 abstract</p> <p>-----</p>	1-13,30

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Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0066631	A	09-11-2000	AT 272073 T	15-08-2004
			AU 768554 B2	18-12-2003
			AU 4588600 A	17-11-2000
			BR 0010162 A	05-02-2002
			CA 2370304 A1	09-11-2000
			DE 60012500 D1	02-09-2004
			EP 1175445 A1	30-01-2002
			EP 1486560 A2	15-12-2004
			ES 2225132 T3	16-03-2005
			WO 0066631 A1	09-11-2000
			GB 2350612 A , B	06-12-2000
			JP 2003501348 T	14-01-2003
			MX PA01010739 A	20-08-2003
			NO 20015261 A	21-12-2001
			NZ 514759 A	31-10-2003
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WO 9713844	A	17-04-1997	AT 190650 T	15-04-2000
			AT 199091 T	15-02-2001
			AU 702049 B2	11-02-1999
			AU 7140596 A	30-04-1997
			CA 2233042 A1	17-04-1997
			DE 69607191 D1	20-04-2000
			DE 69607191 T2	28-09-2000
			DE 69611766 D1	15-03-2001
			DE 69611766 T2	02-08-2001
			DK 945464 T3	07-05-2001
			EP 0853661 A1	22-07-1998
			EP 0945464 A1	29-09-1999
			ES 2146020 T3	16-07-2000
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			WO 9713844 A1	17-04-1997
			GB 2305921 A , B	23-04-1997
			GR 3033436 T3	29-09-2000
			GR 3035775 T3	31-07-2001
			JP 2000500643 T	25-01-2000
			PT 853661 T	31-08-2000
			PT 945464 T	31-07-2001
			US 2005049403 A1	03-03-2005